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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/928,047

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5322120006

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01/14/2004

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EXAMINER

JIANG, DONG

ART UNIT

PAPER NUMBER

1646

DATE MAILED: 01/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/928,047

Applicant(s)

CANTOR, THOMAS L.

Examiner

Dong Jiang

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1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 October 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-8 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 10/15/02. 6) ☐ Other:

DETAILED OFFICE ACTION

Applicant's species election of PTH₇₋₈₄ filed on 10 October 2003 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Upon reviewing the present claims, requirement for the species restriction is withdrawn. Currently, claims 1-8 are pending and under consideration.

Formal Matters:***Sequence***

A sequence error is found in the CRF submitted by the applicants. The error is: the amino acid Asparagine (N) at the position 71 of hPTH (1-84) present in the CRF as SEQ ID NO:1 should be the amino acid Aspartic acid (D) according to the published sequence of hPTH, which is represented by Figure 1 in the instant specification. The same error is present in all sequences in the CRF. Appropriate correction is required.

Specification

The specification is objected to as containing incomprehensible statement. The following items are not understood: "a ... peptide (CIP) having an amino acid sequence *from between* (SEQ ID No.1 [PTH₂₋₈₄]) and (SEQ ID No.2 [PTH₃₄₋₈₄]) ..." on page 1, lines 10-13 of the specification, for example. It is unclear whether the peptide comprises either SEQ ID NO:1 or SEQ ID NO:2, sequences from both, some other combinations, or a sequence that occurs between, i.e. is flanked by the two. Similar statement is found in other places in the specification, and appropriate correction is required for all of them.

The specification is further objected to for improper recitation format of sequences, "SEQ ID No.1" on page 1, line 12 of the specification, for example. The correct format would be

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“SEQ ID NO:1”. Appropriate correction is required for all improper sequence ID recitations in the specification.

The specification is further objected to for miscited sequences: “(SEQ ID No.2 [PTH₃₄₋₈₄])”, “(SEQ ID No.3 [PTH₃₋₈₄])”, and “(SEQ ID No.4 [PTH₂₈₋₈₄])” in lines 12-13, page 1 of the specification, for example. According to the sequence listing, SEQ ID NO:2 is PTH₃₋₈₄, SEQ ID NO:3 is PTH₃₄₋₈₄, and SEQ ID NO:4 is *not* PTH₂₈₋₈₄, which SEQ ID NO:8. Appropriate correction is required.

Abstract

The abstract is objected to for the same reasons above. Appropriate correction is required.

Objections and Rejections under 35 U.S.C. 112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite for the recitation “a ... peptide (CIP) having an amino acid sequence *from between* PTH₂₋₈₄ (SEQ ID NO:1) and PTH₃₄₋₈₄ (SEQ ID NO:3)” in lines 3-4. It is unclear whether the peptide comprises either SEQ ID NO:1 or SEQ ID NO:3, sequences from both, some other combinations, or a sequence that occurs between, i.e. is flanked by the two. The metes and bounds of the claim, therefore, cannot be determined. Claims 2, 5 and 6 are similarly indefinite.

Claim 1 is further indefinite for the limitation of “*therapeutically* effective”, as it is unclear what “therapeutically effective” is for, i.e., for osteoporosis as indicated in the preamble, for hypercalcemia, or for something else. Claim 5 is similarly indefinite.

Further, Claim 5 recites the limitation “the administration of CAP” in the last line. There is insufficient antecedent basis for this limitation in the claim. Additionally, such a limitation also renders the claim indefinite because there is a lack of method steps. The claim is

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further indefinite because it is unclear whether “a patient that has osteoporosis” has necessarily been treated with CAP as the preamble does not suggest such. If “a patient that has osteoporosis” has not been treated with CAP, it is unclear why hypercalcemia or osteosarcoma is necessarily a problem.

Claim 7 is indefinite because with the addition of a method step to determine the amount of CPA and CIP, it is unclear when such a step should be carried out, and what effect the result from such would have on the method.

The remaining claims are rejected for depending from an indefinite claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is “undue” include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Claims 1-8, as written, read on a *method for treating osteoporosis* using a PTH antagonist (or CIP), wherein a patient is also being treated with a PTH agonist (or CAP). However, the prior art has not established that such a regimen combining an agonist and an antagonist for the same receptor is suitable for treating osteoporosis, although each alone, when used at certain dose range and certain clinical state, can be useful for osteoporosis. Also, it is not a general practice to apply a combination of an agonist and an antagonist of the same receptor for the treatment of a disease in most clinical scenarios, as each would neutralize the effect of the other. The present specification provides one experiment, which merely shows (Figure 2), as expected, that PTH increases the serum calcium over a time period of 2 hours, a PTH antagonist (PTH₇₋₈₄)

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decreases the serum calcium, and an equimolar amount of both remains the serum calcium substantially the same over the same period, and it has no indication as to the effect of the combination of PTH and the antagonist *on osteoporosis*. Such an experiment would not be suitable for determining the effect of any agent on osteoporosis as 2 hours does not provide sufficient time for study of osteoporosis. Further, the specification provides no guidance, nor working example as to how to use the claimed invention for treating osteoporosis. Therefore, it is unpredictable that such a combination therapy is suitable for the claimed clinical application, and undue experimentation is required to determine such prior to using the present invention.

Due to the large quantity of experimentation necessary to determine whether the combination of PTH and its antagonist is therapeutic for osteoporosis, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention that involves a unusual combination of an agonist and an antagonist of the same receptor for the treatment, the state of the prior art that has not established that such a combination therapy would be beneficial for osteoporosis, and the lack of the predictability, undue experimentation would be required of the skilled artisan to use the claimed invention.

Even if the present claims were intended to treat hypercalcemia or osteosarcoma resulted from an administration of CAP in a patient having osteoporosis and treated with CAP, they would not be enabled for the following reasons. As shown in Figure 2 of the specification, an equimolar amount of PTH and its antagonist would cause no significant effect on serum calcium levels, and as such, it is highly likely that such a combination would cause no significant net change in other biological effect. Therefore, in order to reduce the occurrence of hypercalcemia or osteosarcoma caused by PTH (or CPA), and to maintain certain effect of PTH treatment on osteoporosis, the amount of the PTH antagonist would be critical. Indeed, claims 1 and 5 define such an amount by reciting “in a therapeutically effective, but non-toxic amount that reduces the occurrence of hypercalcemia or osteosarcoma in the patient”. The amount of the PTH antagonist is defined by its effect. However, as addressed above, prior art has not established such clinical application, and the present specification provides no guidance, nor working example as to how to reduce the occurrence of hypercalcemia or osteosarcoma caused by PTH (or CPA), and to

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maintain certain effect of PTH treatment on osteoporosis. Therefore, undue experimentation would be required of the skilled artisan prior to using the claimed invention.

Prior Art:

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Krstenansky et al. (US 6,051,686, provided by applicants) discloses that PTH agonists are useful in treating osteoporosis (column 2, lines 22-37).

Kanmera et al. (EP 0 451 867 A1) discloses peptide derivatives that are PTH antagonists, and teaches that the derivatives exhibit a potent inhibitory activity against hPTH and are useful as a therapeutic agent for treating dysbolism associated with calcium or phosphoric acid, such as osteoporosis and renal osteodystrophy (the abstract).

Conclusion:

No claim is allowed.

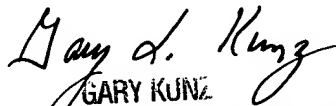
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Advisory Information:

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 703-305-1345. The examiner can normally be reached on Monday - Friday from 9:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.


GARY KUNZ
SUPERVISORY PATENT EXAMINER
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Dong Jiang, Ph.D.
Patent Examiner
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1/6/04